Attorney Docket No.: X-5683B

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re United States Patent No. 4,690,951

Patentees : David B. Anderson et al. Attn: Box Patent Ext.

Assignee : Eli Lilly and Company

Issue Date : September 1, 1987

REQUEST FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. 156

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Pursuant to Section 201(a) of the Drug Price Competition and Patent Term Restoration Act of 1984, 35 U.S.C. 156, Eli Lilly and Company, owner of the above-identified patent by an Assignment recorded on May 21, 1987, in Reel 4714, Frame 572 and on January 26, 1988, in Reel 4824, Frame 524, hereby requests an extension of the patent term of U.S. Patent No. 4,690,951. The following information is submitted in accordance with 35 U.S.C. 156(d) and 37 C.F.R. 1.710 et seq. and follows the numerical format set forth in 37 C.F.R. 1.740(a):

(1) A complete identification of the approved product as by appropriate chemical and generic name, physical structure or characteristics:

The approved product is Paylean™ which is further identified as follows:

Chemical Name

Benzenemethanol, 1-(4-hydroxyphenyl)-2-[1-methyl-3-(4-hydroxyphenyl)propylamino]ethanol hydrochloride [also described in CAS Registry as: 4-hydroxy-alpha-[[[3-(4-hydroxyphenyl)-1-methylpropyl]amino]methyl]-hydrochloride]

Generic Name

Ractopamine hydrochloride

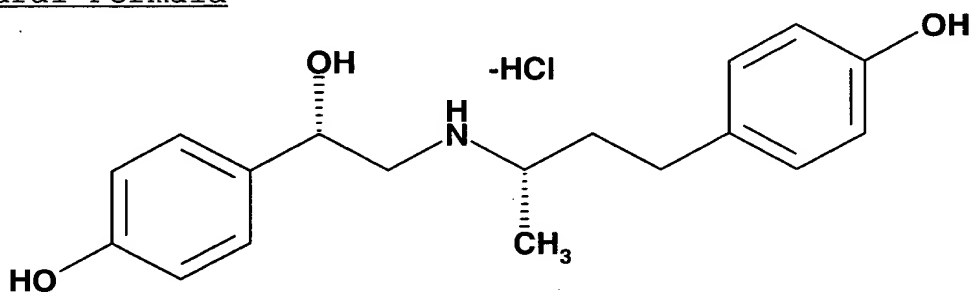
Molecular Formula

$C_{18}H_{23}NO_3$ HCl

Molecular Weight

337.85

Structural Formula



Ractopamine hydrochloride is the active ingredient in the product Paylean™ as may be seen from attached Exhibit I, which is the label for this product.

(2) Paylean™ was subject to regulatory review under section 512 of the Federal Food, Drug and Cosmetic Act (FFDCA), 21 U.S.C. 360(b).

(3) Paylean™ (active ingredient is ractopamine hydrochloride) was approved by the Food and Drug Administration (FDA) for commercial marketing pursuant to Section 512 of the FFDCA on December 22, 1999.

(4) As stated in Sections 1, 2, and 3 above, the active ingredient in the product Paylean™ is ractopamine hydrochloride. Ractopamine hydrochloride has not been approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act prior to approval of NADA 140-863 on December 22, 1999.

(5) The product was approved on December 22, 1999 and the last day within the sixty day period permitted for submission of an application for extension of a patent is February 20, 2000. Since February 20, 2000 is a Sunday, the application may be timely filed on February 21, 2000, the next succeeding business day in accordance with 35 U.S.C. 21. As evident from the Certificate of Mailing by "Express Mail" pursuant to 37 C.F.R. 1.10, this application is timely filed.

(6) The complete identification of the patent for which an extension is being sought is as follows:

U.S. Patent No.:	4,690,951
Inventors:	David B. Anderson, Klaus L. Schmiegel and Edward L. Veenhuizen
Issued:	September 1, 1987
Expires:	September 1, 2004

(7) A copy of U.S. Patent No. 4,690,951, the patent for which extension is being sought, is attached as Exhibit II.

(8) No disclaimer or reexamination certificate has issued for U.S. Patent No. 4,690,951.

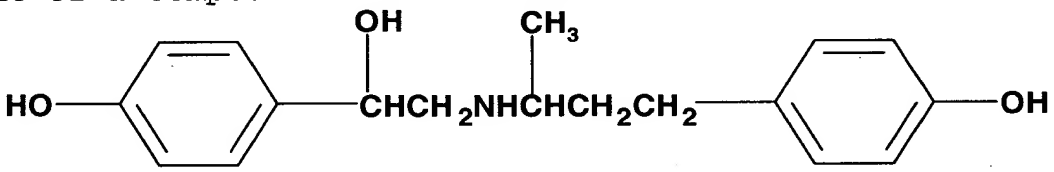
A copy of a certificate of correction that issued for U.S. Patent No. 4,690,951 is attached as Exhibit III. A copy of the maintenance fee statement showing timely payment of fee is attached as Exhibit IV.

(9) A statement that the patent claims the approved product or a method of using or manufacturing the approved product, and a showing which lists each applicable patent claim and demonstrates the manner in which each applicable patent claim reads on the approved product or a method of using or manufacturing the approved product:

U.S. Patent 4,690,951 claims methods of using the approved product. Claims 1, 3 and 4 claim a method of promoting growth of a ruminate by administering the product to the animal. Claims 2, 5 and 6 claim a method of improving the efficiency of feed utilization by ruminants by administering the product to the ruminant. Claims 7, 8 and 9 claim a method for improving leanness in a domesticated animal by administering the approved product to the animal. Accordingly, claims 1-9 all read on approved uses for the product.

Claim 1 reads as follows:

A method for promoting the growth of a ruminant comprising administering to the ruminant a growth promoting amount of a compound of the formula

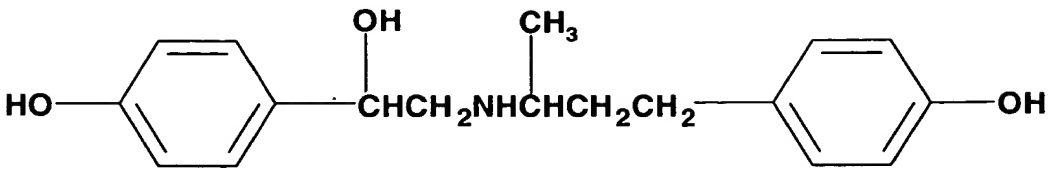


or an acid addition salt thereof.

The approved product is the hydrochloric acid addition salt of the compound shown in the formula. Therefore, claim 1 reads on the approved product.

Claim 2 reads as follows:

A method for improving the efficiency of feed utilization by ruminants comprising administering to the ruminant an effective amount of a compound of the formula



or an acid addition salt thereof.

When the acid addition salt is the hydrochloric acid addition salt, the compound is ractopamine hydrochloride. Therefore, claim 2 reads on the approved product.

Claim 3 of the patent reads as follows:

The method of claim 1 comprising employing 1-(4-hydroxyphenyl)-2-[1-methyl-3-(4-hydroxyphenyl)propylamino]ethanol hydrochloride.

This is ractopamine hydrochloride. Thus, claim 3 reads on the approved product.

Claim 4 of the patent reads as follows:

The method of claim 1 employing R,R-1-(4-hydroxyphenyl)-2-[1-methyl-3-(4-hydroxyphenyl)propylamino]ethanol, or an acid addition salt thereof.

When the acid addition salt is the hydrochloric acid addition salt, the compound is ractopamine hydrochloride. Thus, claim 4 reads on the approved product.

Claim 5 of the patent reads as follows:

The method of claim 2 employing 1-(4-hydroxyphenyl)2-[1-methyl-3-(4-hydroxyphenyl)propylamino]ethanol hydrochloride.

This is ractopamine hydrochloride. Thus, claim 5 reads on the approved product.

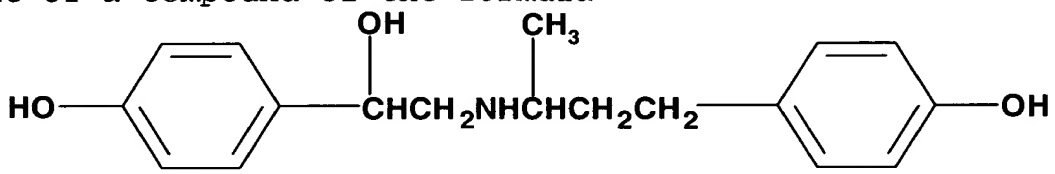
Claim 6 of the patent reads as follows:

The method of claim 2 employing R, R-1-(4-hydroxyphenyl)-2-[1-methyl-3-(4-hydroxyphenyl)propylamino]ethanol, or an acid addition salt thereof.

When the acid is hydrochloric acid, the acid addition salt is ractopamine hydrochloride.

Claim 7 reads as follows:

A method for improving leanness in domesticated animals comprising administering to the animal an effective amount of a compound of the formula



or an acid addition salt thereof.

When the acid is hydrochloric acid, the compound is ractopamine hydrochloride. Thus, claim 7 reads on the approved product.

Claim 8 of the patent reads as follows:

The method of claim 7 employing 1-(4-hydroxyphenyl)-2-[1-methyl-3-(4-hydroxyphenyl)propylamino]ethanol hydrochloride.

This is ractopamine hydrochloride. Thus, claim 8 reads on the approved product.

Claim 9 of the patent reads as follows:

The method of claim 7 employing R,R-1-(4-hydroxyphenyl)-2-[1-methyl-3-(4-hydroxyphenyl)propylamino]ethanol, in an acid addition salt thereof.

When the acid is hydrochloric acid, the addition salt is ractopamine hydrochloride. Thus, claim 9 reads on the approved product.

(10) A statement, beginning on a new page, of the relevant dates and information pursuant to 35 U.S.C. 156(g) in order to enable the Secretary of Health and Human Services or the Secretary of Agriculture, as appropriate, to determine the applicable regulatory review period as follows:

(ii) For a patent claiming a new animal drug, the date a major health or environmental effects test on the drug was initiated and any available substantiation of that date or the date of an exemption under subsection (j) of section 512 of the Federal Food, Drug, and Cosmetic Act became effective for such animal drug; the date on which a new animal drug application (NADA) was initially submitted and the NADA number; and the date on which the NADA was approved:

On April 23, 1984, Eli Lilly and Company, the assignee of U.S. Patent No. 4,690,951, submitted to the FDA a "Notice of Claimed Investigational Exemption for a New Animal Drug" (INAD) under Section 512(j) of the FFDCA to permit the interstate shipment of Paylean™ for the purpose of conducting clinical studies to support the approval of a subsequent NADA for Paylean™. A copy of the letter transmitting the INAD to the FDA is attached as Exhibit V. By letter dated May 9, 1984, the FDA acknowledged receipt of the INAD, assigned the INAD number 4231. A copy of this letter is attached as Exhibit VI. This establishes the beginning of the "regulatory review period" under 35 U.S.C. 156(g)(1) as May 9, 1984, the effective date of an exemption under Section 512(j).

Lilly submitted an NADA for Paylean™, NADA 140-863, on August 27, 1987. A copy of the letter transmitting the NADA is attached as Exhibit VII. The NADA submission was received by the FDA on September 1, 1987 as indicated by Exhibit VIII. Thus, for the purpose of the "regulatory review period" under 35 U.S.C. 156(g)(1), September 1, 1987 is the date of initial submission of a new animal drug application under Section 512 for Paylean™.

The NADA described above was approved on December 22, 1999. Attached as Exhibit IX is a letter dated December 22, 1999 from the FDA to Lilly approving the NADA for Paylean™. Thus, for the purpose of the "regulatory review period" under 35 U.S.C. 156(g)(1), December 22, 1999 is the date of approval of the application for Paylean™ submitted on September 1, 1987.

(11) A brief description beginning on a new page of the significant activities undertaken by the marketing applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities:

During the applicable regulatory review period, Lilly was actively involved in obtaining NADA approval for Paylean™. As discussed in (10) above, the INAD for Paylean™ became effective on May 9, 1984, the NADA was submitted on September 1, 1987, and the NADA was approved on December 22, 1999. Lilly was in close consultation with the FDA during the clinical studies conducted under the INAD. Similarly, subsequent to the submission of the NADA, Lilly had numerous contacts and meetings with the FDA with respect to the approval and, in fact, conducted additional studies at FDA's request to support the NADA approval. The description of significant activities undertaken by Lilly with respect to Paylean™ during the regulatory review period as set forth in Exhibit X is illustrative of the activities involved. Because Applicant is claiming only a three (3) year extension, only very basic information regarding activities during the IND period is presented here but more detailed information regarding this period would be available upon request from the Assistant Commissioner or Secretary.

(12) A statement beginning on a new page that in the opinion of the applicant the patent is eligible for the extension and a statement as to the length of extension claimed, including how the length of extension was determined:

(a) Statement of eligibility of the patent for extension under 35 U.S.C. 156(a):

Section 156(a) provides, in relevant part, that the term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended if (1) the term of the patent has not expired before an application for extension is submitted, (2) the term of the patent has never been extended, (3) the application for extension is submitted by the owner of record of the patent or its agent in accordance with 35 U.S.C. 156(d), (4) the product has been subject to a regulatory review period before its commercial marketing or use, and (5) the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred.

As described below by corresponding number, each of these elements is satisfied here:

(1) The term of U.S. Patent No. 4,690,951 expires on September 1, 2004. This application has, therefore, been submitted before the expiration of the patent term.

(2) The term of this patent has never been extended.

(3) This application is submitted by the owner of record, Eli Lilly and Company (Assignments recorded on May 21, 1987, in Reel 4714, Frame 572, and on January 26, 1988, in Reel 4824, Frame 524). This application is submitted in accordance with 35 U.S.C. 156(d) in that it is submitted

within the sixty day period beginning on the date, December 22, 1999, the product received permission for marketing under the FFDCA and contains the information required under 35 U.S.C. 156(d).

(4) As evidenced by the December 22, 1999 letter from the FDA (Exhibit IX), the product, Paylean™ (ractopamine hydrochloride), was subject to a regulatory review period under Section 512 of the FFDCA before its commercial marketing or use.

(5) Finally, the permission for the commercial marketing of Paylean™ after regulatory review under Section 512 is the first permitted commercial marketing of Paylean™.

This is confirmed by the absence of any approved new drug application for Paylean™ prior to December 22, 1999.

(b) Statement as to length of extension claimed:

The term of U.S. Patent No. 4,690,951 should be extended by 1095 days to September 1, 2007. This extension was determined on the following basis: as set forth in 35 U.S.C. 156(g)(4) and 37 C.F.R. 1.778(c), the regulatory review period equals the length of time between the effective date of the initial INAD, May 9, 1984, and the initial submission of the NADA, September 1, 1987, a period of 1210 days, plus the length of time between the initial submission of the NADA, September 1, 1987, to NADA approval, December 22, 1999, a period of 4495 days. These two periods added together equal 5705 days.

Pursuant to 35 U.S.C. 156(c) and 37 C.F.R. 1.778 (d)(1)(i), the term of the patent eligible for extension shall be extended by the time equal to the regulatory review period which occurs after the date the patent was issued. In this case, this is a period running from the date of patent issue, September 1, 1987, to the date of NADA approval, December 22, 1999, a period of 4495 days.

As discussed in paragraph (11) above and as illustrated in Exhibit X, Lilly was continuously and diligently working toward securing NADA approval for Paylean™. As Lilly acted with due diligence during the entire period of regulatory review, the 4495 day period calculated above as the term of the patent eligible for extension should not be reduced for lack of diligence under 35 U.S.C. 156(c)(1) or 37 C.F.R. 1.775 (d)(1)(ii).

Pursuant to 35 U.S.C. 156(c)(2) and 37 C.F.R. 1.778 (d)(1)(iii), this 4495 day period is to be reduced by one-half of the time from the effective date of the initial INAD May 9, 1984, or the date of patent issue, September 1, 1987, whichever is later, to the date of initial submission of the NADA, September 1, 1987, a period of 0 days. One half of this period is 0 days. Thus, the 4495 day period is reduced by 0 days leaving a revised regulatory period of 4495 days.

Pursuant to 35 U.S.C. 156(c)(3) and 37 C.F.R. 1.778(d)(2-4), if the period remaining in the term of the patent after the date of approval, December 22, 1999, to September 1, 2004, a period of 1706 days), when added to the revised regulatory review period (4495 days) exceeds 14 years (5113 days), the period of extension must be reduced so that the total of both such periods does not exceed fourteen years. In this case, the total of both such periods exceeds 14 years by 1089 days. Therefore, the 4495 day revised regulatory review period must be reduced by 1089 days to a 3407 day period.

As a duplication of the foregoing calculation, the relevant dates and days using 37 C.F.R. 1.778 only are:

1.778(c)(1)	1210 days
1.778(c)(2)	4495 days
1.778(d)(1)(i)	subtract 1210 days
1.778(d)(1)(ii)	subtract 0 days
1.778(d)(1)(ii)	0 days

This leaves a regulatory review period of 4495 days:

1.778(d)(2)	12/22/16
1.778(d)(3)	12/22/13
1.778(d)(4)	12/22/13

The period of patent term extension as calculated above is also subject to the provisions of 35 U.S.C. 156(g)(4) and 37 C.F.R. 1.778(d)(5-6). The patent to be extended issued before and clinical evaluation of the approved product began before November 16, 1987. Since commercial marketing of the drug was approved after enactment of the statute, the three year maximum on extension as provided in 35 U.S.C. 156(g)(6)(C) and 37 C.F.R. 1.778(d)(6)(ii) is applicable. Thus, the term of the patent is eligible for a 1095 day extension until September 1, 2007.

(13) A statement that applicant acknowledges a duty to disclose to the Assistant Commissioner for Patents and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought (See §1.765):

Applicant acknowledges a duty to disclose to the Assistant Commissioner for Patents and the Secretary of Health and Human Services any information which is material to any determination of entitlement to the extension sought. Further to the information already presented in this application and attached exhibits, Applicant notes that U.S. Patent Application Serial No. 628,002 filed July 5, 1984 now abandoned, which is the parent to application Serial Number 811,059 from which U.S. Patent 4,690,951 matured, was also the basis of a continuation application Serial Number 860,719. This continuation application issued as U.S. Patent No. 4,734,437 on March 29, 1988 contains method of use claims embracing the approved product (Paylean™) for promoting growth of swine. A copy of this patent is attached as Exhibit XI. In

addition, Applicant filed and has pending INAD 4304, effective date August 22, 1984, for similar indications to that now approved for Paylean™ (ractopamine hydrochloride).

U.S. Patent Application Serial No. 153,640, filed on February 8, 1988, is a divisional of Serial No. 860,719 and matured as U.S. Patent No. 4,849,453 on July 18, 1989. This patent has method of use claims for raising a meat producing animal and feedstuff claims embracing the approved product Paylean™. A copy of this patent is attached as Exhibit XII. U.S. Application Serial No. 328,996, filed on March 27, 1989, a division of Serial No. 153,640 and issued as U.S. Patent 4,992,473. This patent contains method of use claims embracing the approved product Paylean™ for use in promoting growth of poultry. A copy of this patent is attached as Exhibit XIII. U.S. Patent Application Serial No. 378,789, filed on March 18, 1993, is a continuation of Serial No. 606,670, filed on October 31, 1990, now abandoned, which was a division of Serial No. 328,996. Application Serial No. 378,789 matured as U.S. Patent No. 5,643,967 which contains method of use claims embracing the approved product Paylean™ for use in promoting growth of a domesticated warm blooded animal other than a ruminant. A copy of this patent is attached as Exhibit XIV.

(14) The prescribed fee for receiving and acting upon the application for extension (See §1.20(j)):

As indicated by the letter of transmittal submitted with this application, the Assistant Commissioner for Patents has been authorized to charge the filing fee of $1,120.00 and any additional fees which may be required by this or any other related paper, or credit any overpayment to Deposit Account No. 05-0840] in the name of Eli Lilly and Company and any additional fees which may be required.

(15) The name, address, and telephone number of the person to whom inquiries and correspondence relating to the application for patent term extension are to be directed:

Address all correspondence to Frederick D. Hunter, Eli Lilly and Company, Patent Division/FDH, Lilly Corporate Center, Indianapolis, Indiana 46285. Direct telephone calls to Frederick D. Hunter, 317-433-4101.

(16) A duplicate of the application papers, certified as such:

The undersigned hereby certifies that this application for extension of patent term under 35 U.S.C. 156, including its attachments and supporting papers, is being submitted with a duplicate copy thereof.

(17) An oath or declaration as set forth in 37 C.F.R. 1.740(b):

As the undersigned attorney of Eli Lilly and Company, the owner of record of U.S. Patent No. 4,690,951, which, by submission of this paper and attached Exhibits, now applies for an extension of term of this patent, I, Frederick D. Hunter, declare that (1) I am a Patent Attorney authorized to practice before the Patent and Trademark Office and have general authority from Eli Lilly and Company to act on its behalf in patent matters; that (2)
I have reviewed and understand the contents of this application for extension of U.S. Patent No. 4,690,951 that (3) I believe the patent is subject to extension pursuant to 37 C.F.R. 1.710; that (4) I believe the length of extension claimed is fully justified under 35 U.S.C. 156 and applicable regulations; and that (5) I believe the patent for which this extension is being sought meets the conditions for extension of the term of a patent as set forth in 37 C.F.R. 1.720.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and, further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent extension issuing thereon.

I hereby appoint as United States attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Attorney	Reg. No.	Attorney	Reg. No.
Arvie J. Anderson	45,263	James J. Kelley	41,888
Lynn D. Apelgren	P45,341	Paul C. Kimball	34,641
Robert A. Armitage	27,417	Paul J. Koivuniemi	31,533
Brian P. Barrett	39,597	Robert E. Lee	27,919
Michael T. Bates	34,121	James P. Leeds	35,241
Roger S. Benjamin	27,025	Nelsen L. Lentz	38,537
William R. Boudreaux	35,796	Ronald S. Maciak	35,262
Steven P. Caltrider	36,467	Janet T. McClain	36,863
Paul R. Cantrell	36,470	Scott A. McNeil	37,185
Charles E.Cohen	34,565	Arlene K. Musser	37,895
Kenneth J. Collier	34,982	Douglas K. Norman	33,267
Daniel W. Collins	31,912	Arleen Palmberg	40,422
Robert A. Conrad	32,089	Raymond S. Parker III	34,893
Elizabeth A. Dawalt	44,646	Thomas G. Plant	35,784
Paul R. Darkes	33,862	James J. Sales	33,773
Steven G. Davis	39,652	Michael J. Sayles	32,295
John C. Demeter	30,167	Robert L. Sharp	P45,609
Manisha A. Desai	43,585	David M. Stemerick	40,187
John H. Engelmann	28,075	Mark J. Stewart	43,936
Joanne Longo Feeney	35,134	Robert D. Titus	40,206
Paul J. Gaylo	36,808	Barbara Twardzik	36,386
Francis O. Ginah	44,712	MaCharri Vorndran-Jones	36,711
Edward P. Gray	30,638	Gilbert T. Voy	43,972
Amy E. Hamilton	33,894	Andrea C. Walsh	34,988
Suzanne M. Harvey	42,640	Thomas D. Webster	39,872
Frederick D. Hunter	26,915	Lawrence T. Welch	29,487
Thomas E. Jackson	33,064	Alexander Wilson	P45,782
Charles Joyner	30,466		

retaining for myself to have in addition the power to revoke

the power granted to all others listed above except that to Robert A. Armitage.

ELI LILLY AND COMPANY

By: Frederick D. Hunter

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Attorney for Applicants
Registration No. 26,915
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February 17, 2000